2.0 DESCRIPTION OF PROPOSED RESEARCH IN NON-TECHNICAL LANGUAGE

Cystic fibrosis (CF), the most common inherited disease in North America, is caused by problems in a gene known as “CFTR”. Normal functioning of this gene is required for the movement of water and salt across airway cells. Persons with this disease have abnormal mucous in their lungs which builds up over time and leads gradually, over many years, to serious lung disease. Attempts are being made to replace the missing gene function using special gene carriers, or vectors, which carry corrected genes into cells. The types of vectors tested in patients have so far, had a temporary effect and therefore may not be ideal for treating CF lung disease. Targeted Genetics Corporation has developed a different type of vector, called tgAAVCF, which is based on a virus, AAV. Many people have been infected by the naturally occurring type of AAV without realizing it, as AAV does not cause disease. AAV is able to maintain its DNA for long periods of time in the cells that it enters. This vector may slow or stop lung destruction seen in cystic fibrosis patients. Tests of AAV vectors carrying the CFTR gene have shown it to be biologically active in cells in the test tube and in animals. This vector has been given to 60 patients without serious side effects.

The study described herein proposes to administer a single dose of tgAAVCF to three groups of five adult CF patients. One of these groups will receive no pretreatment, while the other two groups have two different pretreatment regimens. Measurements will be taken to determine if patients in one or more groups have more of the tgAAVCF vector in their lungs, and if it is active. Once enrolled, patients will undergo a screening evaluation prior to having an induced sputum and baseline bronchoscopy on study day 0. The pretreatment regimen will begin on study day 14, and induced sputum collected on study days 14 and 27. tgAAVCF will be administered on study day 28. Patients will be followed up for safety evaluation and induced sputum collection on study day 42. Bronchoscopy and safety evaluations will be performed on study day 56. Patients will be involved in study procedures for a total of 10 weeks.